

This listing of claims will replace all prior versions, and listing of claims in the application.

**Listing of Claims:**

1. (currently amended) A ~~human-compatible~~ humanized monoclonal antibody which is specific for human CD28 and activates human T-lymphocytes of several to all sub-groups without being artificially crosslinked with a secondary antibody and without occupancy of an antigen receptor of the human T-lymphocytes and thus antigen-non-specifically, and which is effective for treating a disease with pathologically reduced number of CD4 T-cells or an autoimmune disease.
2. (previously presented) A monoclonal antibody according to claim 1 which is available through:
  - a) production of hybridoma cells enabled to produce monoclonal human-CD28 specific animal antibodies by means of an immunization with non- T tumor cells on which human CD28 is expressed,
  - b) optionally, humanization of the monoclonal animal antibodies from the hybridoma cells pursuant to a) above through a biochemical or gene-technological exchange of constant components of the animal antibodies against analogous constant components of a human antibody or replacement of genes of the hybridoma cells corresponding to the components; and
  - c) secreting the monoclonal antibodies in a hybridoma cell culture and isolation of the monoclonal antibodies from it or production of the monoclonal antibodies by injection of the hybridoma cells into animals, and isolation of the monoclonal antibodies from the body fluid of the animals.
3. (previously presented) A monoclonal antibody according to claim 1, with the hybridoma cells enabled to produce monoclonal human-CD28 specific animal antibodies being available through

- a) creation of a plasmid by means of insertion of human-CD28 cDNA into the pH $\beta$ APr-1-neo vector following excision of the Sall-HindIII fragment and production of protoplasts from Escherichia coli (MC1061) which carry the plasmid,
- b) fusing of the protoplasts with mouse A20J and/or L929 tumour cells using polyethylene glycol,
- c) cultivation of the transfected cells received in b) above,
- d) screening of the transfected mouse A20J and/or L929 cells for the expression of human CD28 and selection of mouse A20J and/or L929 cells expressing human-CD28,
- e) immunization of BALB/c mice with mouse A20J and/or L929 cells expressing human-CD28,
- f) removal of spleen cells of the mice immunized in this way and fusing the spleen cells with cells of the cell line X63-Ag 8.653 by means of polyethylene glycol to produce the hybridoma cells,
- g) selection of the hybridoma cells produced in f) above with the condition that in the supernatant of selected hybridoma cells there are antibodies contained which bind on human CD28 expressing mouse A20J and/or L929 cells, and
- h) cultivation/sub-cloning of the selected hybridoma cells obtained in g) above and isolating the monoclonal antibodies.

4. (previously presented) A hybridoma cell for the production of a monoclonal antibody according to claim 1, which is available through the following:

- a) creation of a plasmid by means of insertion of human-CD28 cDNA into the pH $\beta$ APr-1-neo vector following excision of the Sall-HindIII fragment and production of protoplasts from Escherichia coli (MC1061) which carry the plasmid,
- b) fusing of the protoplasts with mouse A20J and/or L929 tumour cells using polyethylene glycol,

- c) cultivation of the transfected cells received in b) above,
- d) screening of the transfected mouse A20J and/or L929 cells for the expression of human CD28 and selection of mouse A20J and/or L929 cells expressing human-CD28,
- e) immunization of BALB/c mice with mouse A20J and/or L929 cells expressing human-CD28,
- f) removal of spleen cells of the mice immunized as in e) above and fusing the spleen cells with cells of the cell line X63-Ag 8.653 by means of polyethylene glycol, and
- g) selection of the hybridoma cells received in this way with the condition that in the supernatant of selected hybridoma cells there are antibodies contained which bind on human CD28 expressing mouse A20J and/or L929 cells.

Claims 5-12 are withdrawn.

13. (previously amended) A monoclonal antibody according to claim 2, enabled to produce monoclonal human-CD28 specific animal antibodies being available through

- a) creation of a plasmid by means of insertion of human-CD28 cDNA into the pH $\beta$ APr-1-neo vector following excision of the SalI-HindIII fragment and production of protoplasts from Escherichia coli (MC1061) which carry the plasmid,
- b) fusing of the protoplasts with mouse A20J and/or L929 tumour cells using polyethylene glycol,
- c) cultivation of the transfected cells received in b) above,
- d) screening of the transfected mouse A20J and/or L929 cells for the expression of human CD28 and selection of mouse A20J and/or L929 cells expressing human-CD28,
- e) immunization of BALB/c mice with mouse A20J and/or L929 cells expressing human-CD28,
- f) removal of spleen cells of the mice immunized as in e) above and fusing

the spleen cells with cells of the cell line X63-Ag 8.653 by means of polyethylene glycol to produce the hybridoma cells,

- g) selection of the hybridoma cells received as in f) above with the condition that in the supernatant of selected hybridoma cells there are antibodies contained which bind human CD28 expressing mouse A20J and/or L929 cells, and
- h) cultivation/sub-cloning of the selected hybridoma cells obtained in g) above and isolating of the antibodies therefrom.

14. (previously amended) A hybridoma cell for the production of a monoclonal antibody according to claim 2 which is available through the following:

- a) creation of a plasmid by means of insertion of human-CD28 cDNA into the pHBAPr-1-neo vector following excision of the Sall-HindIII fragment and production of protoplasts from Escherichia coli (MC1061) which carry the plasmid,
- b) fusing the protoplasts with mouse A20J and/or L929 tumour cells using polyethylene glycol,
- c) cultivation of the transfected cells received in b) above,
- d) screening of the transfected mouse A20J and/or L929 cells for the expression of human CD28 and selection of mouse A20J and/or L929 cells expressing human-CD28,
- e) immunization of BALB/c mice with mouse A20J and/or L929 cells expressing human-CD28,
- f) removal of spleen cells of the mice immunized in this way and fusing the spleen cells with cells of the cell line X63-Ag 8.653 using polyethylene glycol, and
- g) selection of the hybridoma cells received as in e) above with the condition that in the supernatant of selected hybridoma cells there are antibodies contained which bind human CD28 expressing mouse A20J and/or L929 cells.

15. (previously amended) A hybridoma cell for the production of a monoclonal antibody according to claim 3 which is available through the following:

- a) creation of a plasmid by means of insertion of human-CD28 cDNA into the pH $\beta$ APr-1-neo vector following excision of the Sall-HindIII fragment and production of protoplasts from Escherichia coli (MC1061) which carry the plasmid,
- b) fusing of the protoplasts with mouse A20J and/or L929 tumour cells using polyethylene glycol,
- c) cultivation of the transfected cells received in b) above,
- d) screening of the transfected mouse A20J and/or L929 cells for the expression of human CD28 and selection of mouse A20J and/or L929 cells expressing human-CD28,
- e) immunization of BALB/c mice with mouse A20J and/or L929 cells expressing human-CD28,
- f) removal of spleen cells of the mice immunized as in e) above and fusing the spleen cells with cells of the cell line X63-Ag 8.653 using polyethylene glycol, and
- g) selection of the hybridoma cells received in this way with the condition that in the supernatant of selected hybridoma cells there are antibodies contained which bind human CD28 expressing mouse A20J and/or L929 cells.

Claim 16-23 are withdrawn.

24. (previously amended) A hybridoma cell for the production of a monoclonal antibody according to claim 13 which is available through the following:

- a) creation of a plasmid by means of insertion of human-CD28 cDNA into the pH $\beta$ APr-1-neo vector following excision of the Sall-HindIII fragment and production of protoplasts from Escherichia coli (MC1061) which carry the plasmid,
- b) fusing of the protoplasts with mouse A20J and/or L929 tumour cells using

- polyethylene glycol,
- c) cultivation of the transfected cells received in b) above,
  - d) screening of the transfected mouse A20J and/or L929 cells for the expression of human CD28 and selection of mouse A20J and/or L929 cells expressing human-CD28,
  - e) immunization of BALB/c mice with mouse A20J and/or L929 cells expressing human-CD28,
  - f) removal of spleen cells of the mice immunized as in e) and fusing the spleen cells with cells of the cell line X63-Ag 8.653 using polyethylene glycol, and
  - g) selection of the hybridoma cells received in this way with the condition that in the supernatant of selected hybridoma cells there are antibodies contained which bind human CD28 expressing mouse A20J and/or L929 cells.

Claims 25-40 are withdrawn.

41. (original) The monoclonal antibody of claim 1, wherein said antibody can be administered to a patient to treat a disease which is characterized by an excessively low T-lymphocyte activity.

42. (original) The monoclonal antibody of claim 1, wherein said disease is AIDS or a leukemic disease.

43. (new) A humanized monoclonal antibody which is specific for human CD28 and which causes T-cell proliferation upon binding to said CD28 on all classes of said T-cells,

wherein said T-cell proliferation is caused without said antibody being artificially crosslinked with a secondary antibody, without occupancy of an antigen receptor of the human T-lymphocytes, and without T-cell receptor stimulation, whereby said T-cell proliferation is caused antigen-non-specifically.

44. (new) An antibody of claim 1, wherein said antibody reacts with human CD28 which is present on non-T-cell tumor cells expressing human CD28.

45. (new) An antibody of claim 1, wherein said antibody reacts with human CD28 which is present on murine A20J or L929 cells expressing human CD28.

46. (new) An antibody of claim 1, which is monoclonal antibody CMY-2 produced by the hybridoma cell line DSM ACC 2353.